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Potential role of glutathione S-transferase M1 gene polymorphism in kidney calcium oxalate stone formation

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Abstract

Background The purpose of this study was to look into the effects of glutathione S-transferase M1 (*GSTM1*) gene polymorphism on the formation of kidney calcium oxalate stones.

Methods A total of 159 patients with kidney calcium oxalate stones were included in this study as a case group. One hundred and three healthy individuals were included in the control group. The age, gender, and levels of calcium (Ca), uric acid (UA), creatinine (Cr), and urinary creatinine (Ucr) are tracked. Peripheral blood samples are used to perform a polymerase chain reaction to identify the glutathione S-transferase (GST) gene polymorphism (PCR). A commercial kit was used in this study to measure the levels of malondialdehyde (MDA), nitric oxide (NO), total antioxidant capacity (T-AOC), and 8-hydroxydeoxyguanosine (8-OHdG) in peripheral blood.

Results There was no difference in age or gender distribution between the case and control groups ($P > 0.05$). The Cr, Ucr, Ca, UA, 8-OHdG, MDA, NO, and T-AOC in the case group were significantly higher than those in the control group ($P < 0.001$). The Hardy–Weinberg genetic equilibrium test showed no difference between the case group ($P = 0.23$) and the control group ($P = 0.09$). In the case group, the 8-OHdG and NO in GSTM1 null genotype were significantly higher than those in GSTM1 genotype ($P < 0.05$), but there was no significant difference in MDA and T-AOC ($P > 0.05$). Multivariate regression analysis showed that the *GSTM1* null genotype was positively correlated with 8-OHdG ($P < 0.001$) and NO ($P < 0.001$).

Conclusions *GSTM1* gene polymorphism might be a detecting risk factor for kidney calcium oxalate stone formation.

Trial registration ChiCTR2100051300.

Keywords Oxidative stress · Glutathione S-transferase · Kidney stones · Calcium oxalate · GSTM1

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Introduction

One typical urinary condition is kidney stones. The development of kidney stones is a complicated and multifactorial condition that involves the interaction of environmental and genetic factors [1]. More and more evidence shows that inflammation, oxidation–antioxidation imbalance, angiogenesis, and other factors may play a key role in the occurrence and development of renal stones [2]. Some views suggest that the origin of calcium oxalate stone is closely related to the excessive production of ROS mediated by oxidative stress [3]. This may be due to excessive reactive oxygen species that lead to the transformation of epithelial cells into osteoblasts and the remodeling of the extracellular matrix (ECM), which promotes the deposition of calcium phosphate [4] on the basement membrane of renal tubules or blood vessels. Continuous exposure of renal epithelial cells to high levels of oxalate and calcium oxalate crystals can lead to cell damage and oxidative stress, such as increased free radical production, increased lipid peroxidation, and decreased cellular antioxidant status [5]. Studies have shown that during the formation of calcium oxalate stone, 8-hydroxydeoxyguanosine (8-OHdG) and malondialdehyde (MDA) increased, while total antioxidant capacity (T-AOC), superoxide dismutase (SOD), and glutathione (GSH) decreased, which confirmed the existence of DNA damage and lipid peroxidation caused by oxidative stress [6]. In addition, a number of studies have also confirmed that increasing antioxidants (SOD, GSH, and catalase) can effectively protect renal epithelial cells from calcium oxalate stones [5, 7, 8].

In particular, glutathione S-transferase (GSTs) helps maintain intracellular redox balance and protect DNA from damage by catalyzing the binding of reduced glutathione to ROS, carcinogens, and their metabolites. There are five known types of GSTs, including alpha, u, theta, pi, and zeta in humans [9]. The polymorphism of their alleles will result in differences in enzyme activity [9–11]. The *GSTP1*-I105V polymorphism is caused by the A-G substitution at the base binding site of the exon, resulting in the transformation of the 105th amino acid of the protein–peptide chain from ATC isoleucine (Ile) to GTC valine (Va1) [12]. This change will reduce the activity and thermal stability of the enzyme. Allele deletion is the main cause of *GSTT1* and *GSTM1* gene polymorphism, and the genetic deletion of this gene will lead to the loss of enzyme activity phenotype [13]. The DNA changes in these individuals are called single-nucleotide polymorphisms (SNPs). One of the reasons why SNPs are not uncommon in human individuals is the loss of gene methylation. In particular, *GSTM1* is considered to be a potential candidate regulator of renal vascular injury in recent years, so it is defined as an important factor in the progression of renal disease [14]. Previous studies have shown that the absence of *GSTM1* will lead to an increase in oxidative stress, inflammation, and injury in the kidney, suggesting that other GST pathways may lack the ability to combat oxidative stress in renal vessels [15]. Therefore, we speculate that *GSTM1* may play an important role in the pathogenesis of renal calculi by regulating oxidative stress.

The current work aimed to determine whether *GSTM1* gene polymorphism is associated with the occurrence of renal calculi.

Methods

Study subjects

A total of 159 patients with kidney stones were included in the case group, in accordance with the European Association of Urology (EAU) urolithiasis guidelines (updated 2022) (https://uroweb.org/guidelines/urolithiasis). All patients required PCNL therapy, and calcium oxalate was the main finding in the postoperative stone analysis. The control group included 200 healthy individuals with no history of urolithiasis and no family history of urolithiasis.

Exclusion standards such as 1. poor diet, excess weight, hyperuricemia, dyslipidemia, and parathyroid dysfunction; 2. metabolic syndrome, high blood pressure, diabetes, gout, severe respiratory conditions, chronic heart failure, chronic kidney illness, severe gastrointestinal conditions, and hyperthyroidism or hypothyroidism; and 3. patients who recently underwent blood transfusion therapy, have a history of urolithiasis, or have urolithiasis in their family should be properly watched.

Using a questionnaire, clinical information such as age, prior medical history, family history, height, weight, and blood pressure was gathered. Using computed tomography or ultrasonography, kidney stones were identified (CT). Creatinine (Cr), uric acid (UA), calcium (Ca), serum triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and fasting blood glucose were all measured in peripheral venous blood (FBG). For the urine creatinine (Ucr) test, urine was used. Statistics were examined for sex, age, blood creatinine, uric acid, calcium, and urine creatinine.

Detection of gene polymorphism

GSTM1 genotypes were detected by multiplex polymerase chain reaction (PCR) using primer sequences published by GENEWIZ (Suzhou) Biotechnology, as mentioned earlier [16]. The primers and products were summarized as follows.

The primer used was *GSTM1 (p*ositive, 5′-GAACTCCCT GAAAAGCTAAAGC-3′; reverse, 5′-GTTGGGCTCAAA TATACGGTGG-3′), and the PCR product of the *GSTM1* gene was a fragment of 215 bp. The marker used was DNA Ladder (Solarbio Science & Technology, Beijing).

NO, MDA, 8-OHdG, and TAC detection

Nitric oxide (NO), total antioxidant capacity (T-AOC), 8-OHdG, and malondialdehyde (MDA) levels in plasma were measured using colorimetric techniques and a spectrophotometer (BioMate 5, Thermo Electron Corporation, Rochester, NY, USA). The assays were carried out using the assay kits acquired from the Nanjing Jiancheng Institute of Bioengineering in accordance with the manufacturer's instructions (Nanjing, China).

The statistical analysis was carried out using SPSS 22.0 (SPSS, Inc., Chicago, Illinois, USA). All data were expressed as mean ± standard deviation (mean ± SD), an independent-samples *t*-test was used to compare the two groups of data, the chi-square goodness-of-fit test was used to verify the Hardy–Weinberg balance, and multiple linear regression analysis was used to analyze the correlation. $P < 0.05$ was considered to be statistically significant.

Results

Age and sex distribution between the case group and control group did not change ($P > 0.05$). The case group's levels of Cr, Ucr, Ca, UA, UA/Cr, and Ca/Cr were considerably greater than those in the control group ($P < 0.001$), suggesting that the case group may have had a more pronounced kidney injury (Table 1).

The results in Table 2 showed that *GSTM1* was positively correlated with renal calcium oxalate. The susceptibility to stone in the *GSTM1* null type increased by 2.213 times, and its distribution frequency in the case group and the control group was 60.31% and 40.78%, respectively. The patients in the study underwent the Hardy–Weinberg genetic equilibrium test of genotype distribution, and no differences were discovered between the case group and the control group ($P = 0.23$ and $P = 0.09$, respectively) (Table 3).

Table 2 Frequency distribution of genetic polymorphism of GSTM1 gene in the normal control group and the case group

Gene type	Controls (no. (%))	Patients (no. (%))	OR	95% CI
GSTM1				
(+)	61(51.22)	63(39.66)		
(–)	42(40.78)	96(60.34)	2.213	1.335–3.669

Abbreviations: + present genotype, – null genotype, *95% CI* 95% confidence interval, *OR* odds ratio

There were significant changes in 8-OHdG ($P < 0.001$), MDA ($P < 0.001$), NO ($P < 0.001$), and T-AOC ($P < 0.001$) between the control group and the case group. In the case group, oxidative stress appeared to be more severe. There were no significant changes in MDA ($P = 0.12$) or T-AOC ($P = 0.053$) when the *GSTM1* genotypes of the case group were compared, although there were significant differences in 8-OHdG ($P < 0.001$) and NO ($P < 0.05$). According to this, the *GSTM1* null group was more severely affected by oxidative stress (Table 4).

The *GSTM1* null genotype was favorably connected with 8-OHdG ($P < 0.001$) and NO ($P < 0.001$), according to multivariate regression analysis, but it was not significantly correlated with MDA ($P = 0.102$), T-AOC ($P = 0.053$), Cr ($P = 0.31$), Ucr ($P = 0.882$), UA ($P = 0.926$), or Ca ($P = 0.709$). It appeared that the *GSTM1* null gene had no discernible impact on the level of antioxidants in general (Table 5).

Table 1 Clinical characteristics of the study subjects

Group	N	Male (n%)	Age (years)	Cr (μmol/L)	Ucr (mmol/d)	Ca (mmol/L)	UA (mg/dl)	UA/Cr	Ca/Cr
Controls	103	52(50.5%)	47.2 ± 19.3	72.29 ± 5.27	9.63 ± 2.14	2.33 ± 0.07	4.46 ± 0.62	0.062 ± 0.009	0.032 ± 0.002
Cases	159	84(52.8%)	48.2 ± 18.1	77.94 ± 6.92	10.99 ± 2.57	2.34 ± 0.08	4.45 ± 0.71	0.057 ± 0.008	0.030 ± 0.002
P value		P > 0.05[a]	P > 0.05[a]	*P* < 0.001[a]	*P* < 0.001[a]	*P* < 0.001[a]	*P* < 0.001[a]	*P* < 0.001[a]	*P* < 0.001[a]
GSTM1									
(+)	63	28(44.4%)	49.2 ± 17.3	76.98 ± 7.68	10.94 ± 2.14	2.33 ± 0.08	4.42 ± 0.72	0.057 ± 0.008	0.031 ± 0.003
(–)	96	42(43.8%)	51.2 ± 15.8	78.57 ± 6.34	11.03 ± 2.84	2.35 ± 0.08	4.48 ± 0.70	0.058 ± 0.009	0.030 ± 0.002
P value		*P* > 0.05[b]	*P* > 0.05[b]	*P* > 0.05[b]	*P* > 0.05[b]	*P* > 0.05[b]	*P* > 0.05[b]	*P* > 0.05[b]	*P* > 0.05[b]

Cr blood creatinine, *Ca* blood calcium, *UA* blood uric acid, *Ucr* urine creatinine, (+) *GSTM1* genotype, (–) *GSTM1* null genotype

[a]Comparison between the case group and the control group

[b]Comparison between *GSTM1*(+) and GSTM (–) in the case group

Table 3 Hardy–Weinberg genetic equilibrium test for the distribution of *GSTM1* genotypes

Group	N	Genotypes			χ^2	*P* value
		CC	CT	TT		
Control	103	18	43	42	1.41	0.23
Case	159	13	50	96	2.92	0.09

Table 4 Comparison of 8-OHdG, MDA, NO, and T-AOC

Group	N	8-OHdG	MDA	NO	T-AOC
Control	103	21.68 ± 13.56	38.54 ± 5.39	40.87 ± 6.25	41.27 ± 5.61
Case	159	40.65 ± 17.37	48.23 ± 6.35	61.33 ± 4.67	30.18 ± 5.37
GSTM1 (+)	63	31.56 ± 11.35	46.95 ± 8.37	55.23 ± 6.76	31.51 ± 4.95
GSTM1 (–)	96	49.54 ± 16.58	50.61 ± 9.35	63.97 ± 8.21	29.49 ± 6.38
P-value[a]		< 0.001	< 0.001	< 0.001	< 0.001
P-value[b]		< 0.001	< 0.001	< 0.001	< 0.001
P-value[c]		< 0.001	< 0.001	< 0.001	< 0.001
P-value[d]		< 0.001	0.102	< 0.05	0.053

+ *GSTM1*genotype, – *GSTM1* null genotype, *MDA* malondialdehyde, *8-OHdG* 8-hydroxydeoxyguanosine, *NO* nitric oxide, *T-AOC* total antioxidant capacity

[a]Comparison between the case group and the control group

[b]*GSTM1* genotype in the case group compared with the control group

[c]*GSTM1* null genotype in the case group compared with the control group

[d]Comparison between *GSTM1* and *GSTM1* null genotype in the case group

Table 5 Multiple linear regression analysis of *GSTM1* null genotype in the case group

Outcome	*GSTM1* null		
	B	*P*	95% CI
8-OHdG	0.439	< 0.001	15.134–28.331
MDA	0.132	0.102	− 0.403–4.817
NO	0.289	< 0.001	2.225–5.129
T-AOC	0.121	0.053	− 4.17–0.007
Cr	− 0.29	0.31	0.919–1.027
Ucr	− 0.1	0.882	0.873–1.124
Ca	− 0.927	0.709	0.003–51.958
UA	− 0.024	0.926	0.621–1.689

Cr blood creatinine, *Ca* blood calcium, *UA* blood uric acid, *Ucr* urine creatinine, *MDA* malondialdehyde, *8-OHdG* 8-hydroxydeoxyguanosine, *NO* nitric oxide, *T-AOC* total antioxidant capacity

Discussion

The prevalence of kidney stones is significant and has been rising for several decades [11]. About 80% of kidney stones are calcium oxalate stones, and the mechanism involves the interaction of genes and the environment [17]. Oxidative stress enhances the adhesion and deposition of calcium oxalate on the surface of the renal nipple and causes inflammation and tissue damage, according to in vitro and animal model studies. They encourage one another and ultimately result in the production of kidney stones [18–20]. Overexposure to ROS triggers immune cell activation and damages renal tubular epithelial cells. More crystals remain in the kidney, resulting in stone formation, as a result of the injured cells' increased expression of adhesion molecules. The mitogen-activated protein kinase (MAPK), c-Jun, and nuclear factor kappa B (NF-κB) signal pathways interact throughout this process [21–23]. By preventing the generation and activation of reactive oxygen species, the crystal deposition of inflammatory bodies can be decreased in the investigation of an animal model of calcium oxalate stones. Our analysis found the same pattern. Patients with kidney stones have higher NO and lower T-AOC compared with healthy individuals, as well as a higher overall oxidative stress burden, which may indicate more cell damage.

The enzyme glutathione S-transferase (GST) helps build the antioxidant defense system and keeps cells' redox equilibrium in check [24, 25]. Previous research has demonstrated that the GST gene's polymorphism affects the structure and activity of GST and alters the body's ability to produce antioxidants and OS levels [26, 27]. It has been demonstrated that uric acid helps calcium oxalate crystals form while calcium oxalate stones are developing [28]. The free radicals OH-, ONOO, and others could interact with uric acid. The other radicals they creates, which has potent oxidizing capabilities, exacerbates cell oxidative

damage [29]. OS damages the renal tubular epithelial cells and increases the likelihood of crystal adhesion [30]. In our investigation, patients in the case group who had the *GSTM1* null genotype displayed a higher oxidative stress burden than those who had the *GSTM1* genotype. 8-OHdG and NO were linked with the *GSTM1* null genotype, indicating that patients who have this genotype may have more severe oxidative damage. We hypothesize that the *GSTM1* null genotype may influence the resistance to oxidative stress of renal tubular epithelial cells. More crystals are formed as a result of the weak antioxidant capacity, which may be connected to the development of stones. Although T-AOC is lower in kidney stone patients than in healthy individuals, there is no distinction in T-AOC between the *GSTM1* null and *GSTM1* genotypes in the case group. Through correlation analysis, we discovered that the *GSTM1* null genotype did not correlate with T-AOC. It might have something to do with the antioxidant system's complicated makeup. SOD, GPX, GST, and other exogenous materials such as vitamin C and vitamin E are just a few of the enzymes that make up the human antioxidant system. The overall antioxidant effect may not be significantly impacted by the alteration of certain components. The *GSTM1* null is only a small portion of the overall mechanism that results in the redox imbalance during stone formation. The entire mechanism of kidney stone production cannot be satisfactorily characterized because of the limitations of case–control research. Second, all of the case group participants in our study require surgical intervention. More mechanism investigations are required in future to prove that long-term stone stimulation cannot accurately reflect the small changes in oxidative stress at the early stage of stone formation.

Conclusion

The development of kidney calcium oxalate stones is closely tied to oxidative stress. Compared to healthy persons, patients with calcium oxalate stones displayed a higher load of oxidative stress. One of the major risk factors for kidney calcium oxalate stone development is oxidative stress, which renal tubular epithelial cells may be more susceptible to as a result of the reduction in *GSTM1* enzyme activity brought on by *GSTM1* null.

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Author contributions KT conceived and designed the experiments; PC, JC, SX, TH, ML, WL, and YY performed the experiments; PC and SX analyzed the data; SX wrote the paper; and BC and WZ participated in the discussion.

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Data availability This article contains all of the data generated or analyzed during this investigation.

Declarations

Conflict of interest There are no conflicts of interest declared by the authors.

Ethical statement This research involved human participants, and all the participants provided written informed consent. This research was approved by the Ethics Committee of the Affiliated Hospital of Guizhou Medical University, and all work has been carried out in compliance with the Helsinki Declaration.

Research involving human participants and/or animals The subjects in this study were all humans, and they all gave written informed consent. The Ethics Committee of Guizhou Medical University's Affiliated Hospital gave its approval to this study (trial registration number: ChiCTR-IPR-14005580). Furthermore, every work was completed in accordance with the Helsinki Declaration.

References

1. Yasui T, Okada A, Hamamoto S, Ando R, Taguchi K, Tozawa K et al (2017) Pathophysiology-based treatment of urolithiasis. Int J Urol 24(1):32–38. https://doi.org/10.1111/iju.13187
2. Wigner P, Grebowski R, Bijak M, Szemraj J, Saluk-Bijak J (2021) The molecular aspect of nephrolithiasis development. Cells. https://doi.org/10.3390/cells10081926
3. Khan SR (2014) Reactive oxygen species, inflammation and calcium oxalate nephrolithiasis. Transl Androl Urol 3(3):256–276. https://doi.org/10.3978/j.issn.2223-4683.2014.06.04
4. Bird VY, Khan SR (2017) How do stones form? Is unification of theories on stone formation possible? Arch Esp Urol 70(1):12–27
5. Thamilselvan S, Byer KJ, Hackett RL, Khan SR (2000) Free radical scavengers, catalase and superoxide dismutase provide protection from oxalate-associated injury to llc-pk1 and mdck cells. J Urol 164(1):224–229
6. Zhai W, Zheng J, Yao X, Peng B, Liu M, Huang J et al (2013) Catechin prevents the calcium oxalate monohydrate induced renal calcium crystallization in nrk-52e cells and the ethylene glycol induced renal stone formation in rat. BMC Complement Altern Med 13:228. https://doi.org/10.1186/1472-6882-13-228
7. Song Q, He Z, Li B, Liu J, Liu L, Liao W et al (2020) Melatonin inhibits oxalate-induced endoplasmic reticulum stress and apoptosis in hk-2 cells by activating the ampk pathway. Cell Cycle 19(20):2600–2610. https://doi.org/10.1080/15384101.2020.1810401
8. Selvam R (2002) Calcium oxalate stone disease: role of lipid peroxidation and antioxidants. Urol Res 30(1):35–47. https://doi.org/10.1007/s00240-001-0228-z
9. Acar H, Kilinc M, Guven S, Inan Z (2012) Glutathione s-transferase m1 and t1 polymorphisms in Turkish patients with varicocele. Andrologia 44(1):34–37. https://doi.org/10.1111/j.1439-0272.2010.01103.x
10. Simeunovic D, Odanovic N, Pljesa-Ercegovac M, Radic T, Radovanovic S, Coric V et al (2019) Glutathione transferase p1 polymorphism might be a risk determinant in heart failure. Dis Markers 2019:6984845. https://doi.org/10.1155/2019/6984845

11. Cao T, Xu N, Wang Z, Liu H (2017) Effects of glutathione s-transferase gene polymorphisms and antioxidant capacity per unit albumin on the pathogenesis of chronic obstructive pulmonary disease. Oxid Med Cell Longev 2017:6232397. https://doi.org/10.1155/2017/6232397
12. Buchard A, Sanchez JJ, Dalhoff K, Morling N (2007) Multiplex pcr detection of gstm1, gstt1, and gstp1 gene variants: simultaneously detecting gstm1 and gstt1 gene copy number and the allelic status of the gstp1 ile105val genetic variant. J Mol Diagn 9(5):612–617. https://doi.org/10.2353/jmoldx.2007.070030
13. Strange RC, Jones PW, Fryer AA (2000) Glutathione s-transferase: genetics and role in toxicology. Toxicol Lett 112–113:357–363. https://doi.org/10.1016/s0378-4274(99)00230-1
14. Le TH (2021) Gstm1 gene, diet, and kidney disease: implication for precision medicine?: Recent advances in hypertension. Hypertension 78(4):936–945. https://doi.org/10.1161/HYPERTENSIONAHA.121.16510
15. Gigliotti JC, Tin A, Pourafshar S, Cechova S, Wang YT, Sung SJ et al (2020) Gstm1 deletion exaggerates kidney injury in experimental mouse models and confers the protective effect of cruciferous vegetables in mice and humans. J Am Soc Nephrol 31(1):102–116. https://doi.org/10.1681/ASN.2019050449
16. Liu D, Che B, Chen P, He J, Mu Y, Chen K et al (2022) Gstt1, an increased risk factor for prostate cancer in patients with metabolic syndrome. J Clin Lab Anal 36(4):e24352. https://doi.org/10.1002/jcla.24352
17. Ferraro PM, Bargagli M, Trinchieri A, Gambaro G (2020) Risk of kidney stones: influence of dietary factors, dietary patterns, and vegetarian-vegan diets. Nutrients. https://doi.org/10.3390/nu12030779
18. Khan SR, Pearle MS, Robertson WG, Gambaro G, Canales BK, Doizi S et al (2016) Kidney stones. Nat Rev Dis Primers 2:16008. https://doi.org/10.1038/nrdp.2016.8
19. Yasui T, Iguchi M, Suzuki S, Kohri K (2008) Prevalence and epidemiological characteristics of urolithiasis in Japan: national trends between 1965 and 2005. Urology 71(2):209–213. https://doi.org/10.1016/j.urology.2007.09.034
20. Niimi K, Yasui T, Okada A, Hirose Y, Kubota Y, Umemoto Y et al (2014) Novel effect of the inhibitor of mitochondrial cyclophilin d activation, *n*-methyl-4-isoleucine cyclosporin, on renal calcium crystallization. Int J Urol 21(7):707–713. https://doi.org/10.1111/iju.12425
21. Ma MC, Chen YS, Huang HS (2014) Erythrocyte oxidative stress in patients with calcium oxalate stones correlates with stone size and renal tubular damage. Urology 83(2):510–519. https://doi.org/10.1016/j.urology.2013.09.050
22. Williams J, Holmes RP, Assimos DG, Mitchell T (2016) Monocyte mitochondrial function in calcium oxalate stone formers. Urology 93:221–224. https://doi.org/10.1016/j.urology.2016.03.004
23. Tavasoli S, Taheri M (2019) Vitamin d and calcium kidney stones: a review and a proposal. Int Urol Nephrol 51(1):101–111. https://doi.org/10.1007/s11255-018-1965-z
24. de Oliveira M, Mallmann NH, de Souza G, de Jesus BT, Lima ES, de Lima D et al (2021) Glutathione s-transferase, catalase, and mitochondrial superoxide dismutase gene polymorphisms modulate redox potential in systemic lupus erythematosus patients from Manaus, Amazonas. Brazil Clin Rheumatol 40(9):3639–3649. https://doi.org/10.1007/s10067-021-05680-0
25. Sies H (2021) Oxidative eustress: on constant alert for redox homeostasis. Redox Biol 41:101867. https://doi.org/10.1016/j.redox.2021.101867
26. Ceban E, Banov P, Galescu A, Botnari V (2016) Oxidative stress and antioxidant status in patients with complicated urolithiasis. J Med Life 9(3):259–262
27. Owens L, Laing IA, Murdzoska J, Zhang G, Turner SW, Le Souef PN (2019) Glutathione s-transferase genotype protects against in utero tobacco-linked lung function deficits. Am J Respir Crit Care Med 200(4):462–470. https://doi.org/10.1164/rccm.201807-1332OC
28. Kalaiselvi P, Udayapriya KL, Selvam R (1999) Uric acid-binding proteins in calcium oxalate stone formers and their effect on calcium oxalate crystallization. BJU Int 83(9):919–923. https://doi.org/10.1046/j.1464-410x.1999.00084.x
29. Gherghina ME, Peride I, Tiglis M, Neagu TP, Niculae A, Checherita IA (2022) Uric acid and oxidative stress-relationship with cardiovascular, metabolic, and renal impairment. Int J Mol Sci. https://doi.org/10.3390/ijms23063188
30. Ermak G, Davies KJ (2002) Calcium and oxidative stress: from cell signaling to cell death. Mol Immunol 38(10):713–721. https://doi.org/10.1016/s0161-5890(01)00108-0